Research

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Journal of Rare Disorders: Diagnosis & Therapy
ISSN 2380-7245

2022
Vol.8 No.7:48

Qualitative Investigation of Fatigue and Its Daily Impacts as Perceived By Individuals with Barth Syndrome

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Received date: June 14, 2022, Manuscript No. IPRDDT-22-13670; **Editor assigned date**: June 16, 2022, PreQC No. IPRDDT-22-13670 (PQ); **Reviewed date**: June 29, 2022, QC No. IPRDDT-22-13670; **Revised date**: July 07, 2022, Manuscript No. IPRDDT-22-13670 (R); **Published date**: July 14, 2022, DOI: 10.36648/2380-7245.8.7.48

Citation: Babson I, Daw E, Reynolds S (2022) Qualitative Investigation of Fatigue and Its Daily Impacts as Perceived By Individuals with Barth Syndrome. J Rare Disord Diagn Ther Vol. 8 No.7:48

Abstract

Context: Barth Syndrome is an x-linked, recessive, genetic condition affecting the mitochondria's ability to function correctly within cells causing fatigue. Exactly what it means to be "Barth Tired", however, remains elusive, as does the impact of fatigue on those with BTHS.

Objective: Our objective was to understand how individuals with BTHS perceive and experience fatigue to better understand its impact on daily life functioning.

Design: We used a qualitative study design with a phenomenological approach. Virtual interviews were conducted *via* zoom. Audio recordings of each interview were transcribed and imported into Atlas.ti for analysis and coding. The research team used an inductive process to code the transcripts which informed the development of the themes.

Subjects: Twenty participants, ages 5 years to adult were recruited *via* the Barth Syndrome Foundation (BSF).

Setting: Virtual

Results: Data coding and analysis revealed four primary themes related to the impact of fatigue on individuals with BTHS:

- BTHS fatigue has significant social implications.
- BTHS fatigue manifests itself through cognitive and physical signs and symptoms.
- BTHS fatigue is correlated with an inability to engage in activity leading to limited independence.
- BTHS fatigue requires fatigue management and accommodations.

Conclusion: Findings suggest that fatigue in BTHS may need to be considered not only in terms of muscular endurance, but in a more robust fashion to capture the impact of fatigue on cognitive functioning, social participation, self-care independence, and quality of life. These findings may be used to guide selection of techniques, accommodations, and task-modifications for optimal participation.

Introduction

Barth syndrome is an x-linked, recessive, genetic condition affecting the mitochondria and their ability to function correctly within cells. BTHS is extremely rare and mostly occurs in males; it is estimated that one in every 300,000 to 400,000 individuals are affected globally with approximately 150 cases discussed in scientific literature [1]. Fatigue is a central clinical symptom of BTHS that has been described as one which profoundly limits many aspects of daily life functioning [2]. Exactly what it means to be "Barth Tired", however, remains elusive, as does the impact of fatigue on those with BTHS. This study aimed to understand how individuals with BTHS experience fatigue and their perceptions of fatigue on daily life functioning.

Background

BTHS as a Mitochondrial Disorder

BTHS is caused by mutations within the TAZ gene, located at Xq28, which encodes for the tafazzin protein. Tafazzin is a mitochondrial-localized enzyme, which, when functioning properly works to remodel cardiolipin, a structure crucial to the building and maintenance of the inner mitochondrial membrane [3]. These mutated TAZ genes yield abnormal tafazzin production leading to flawed cardiolipin remodeling and ultimately a compromised inner mitochondrial membrane prohibiting the organelle from functioning properly within the cell [4]. In BTHS, the tissues that make up the most important and hard-working organs and muscles, like the heart and skeletal muscles, are most susceptible to significant mutation and cell death due to the lack of energy production these organs are able to receive from their damaged cell mitochondria [1]. As such, BTHS is classified as a mitochondrial disorder and the symptoms associated with Barth often overlap with other mitochondrial disorders.

Mitochondria are responsible for the production of Adenosine 5'-TriPhosphate (ATP), the chemical energy-carrying molecule which when properly broken-down yields the fuel used to power every cellular process within living things. Though widely known as the energy-producing cells of the body, mitochondria do more than convert ATP into energy. They also play a critical role in insulin secretion, cellular substrate regulation, metabolism, homeostasis, and apoptosis making the consequences of their dysfunction widespread across many aspects of biological functioning [5]. Research has shown that 70-100% of persons with primary mitochondrial diseases report at least moderate fatigue [6-8], while preliminary data in some populations suggests a correlation between disease severity and fatigue severity [7,9]. This fatigue may be perceived fatigue, presented as low energy, exhaustion, or tiredness, or physiological fatigue, presented by exercise intolerance. Presence of symptoms and severity of fatigue may also correlate with rates and severity of mental health disorders such as depression and anxiety, as well as sleep issues in persons with primary mitochondrial diseases. Importantly, research on persons with primary mitochondrial diseases has implicated fatigue as having a role in an individual's ability to complete daily life skills such as personal hygiene, swallowing, and toileting [10,11]. So, although fatigue does not typically present as the most life-threatening physiological symptom of mitochondrial disorders, the literature suggests that there may be an association between fatigue and quality of life [5].

BTHS Phenotype

When studying fatigue in BTHS, it is important to consider that several different mutations have been identified leading to variable clinical presentations [12]. The most ubiquitous characteristics in those diagnosed with BTHS are dilated cardiomyopathy, skeletal myopathy commonly affecting the most proximal muscles, and neutropenia, which is characterized by a severely low white blood cell (neutrophil) count contributing to a weak immune system often resulting in repeated infections. Additional features include delayed motor milestones, abnormal fatigability and exercise intolerance, delayed puberty, and growth delay prior to adolescence. Individuals affected by BTHS historically have shorter life expectancies, often due to serious cardiac complications or the neutropenia causing repeated infections that become more difficult to fight over time [13].

Over the last two decades, there has been a significant influx in research and consequent knowledge surrounding BTHS, stemming in large part from the advocacy and research efforts of the Barth Syndrome Foundation (BSF) formed in the year 2000. A scan of the literature suggests that much of this work has been mechanistic in nature, focused on underlying cellular, metabolic and genetic pathologies with the aim of identifying pharmacological or other therapeutic options (*e.g.*, tafazzin gene replacement therapy, induced pluripotent stem cells) [14-16]. While these advances are essential steps in finding a cure for BTHS, there is still a need to identify relevant therapeutic targets for clinical trials that will alleviate the symptoms of BTHS that are most impactful on quality of life, including fatigue.

While fatigue has received some attention in the broader mitochondrial disorder literature [17], relatively little has been published regarding fatigue specific to BTHS. In studies that have included measures of fatigue, the 6-Minute Walk Test (6MWT) and Sit-to-Stand Test (SST) have been the most commonly used assessments of physical endurance within the BTHS population [15,18-20]. While both tests have been found to be valid and reliable measures of assessing physical functional ability, particularly in cardiac and pulmonary rehabilitation, these measures lack the ability to provide a complete picture of how fatigue impacts daily life function; nor do they consider differing aspects of fatigue such as cognitive or emotional fatigue [21]. Individuals with BTHS are known to have higher rates of perceived tiredness, mental fatigue, sleep problems, and psychosocial concerns like anxiety and depression; all of which are symptoms that have been linked to fatigue in other mitochondrial disorders [22-25]. Research is needed that expands on the current conceptualization of physical/ physiological fatigue in BTHS to examine the multidimensional aspects of fatigue and its impact on daily living in natural environments.

Study Purpose

The purpose of this study was to more fully understand how individuals with BTHS experience fatigue and how fatigue affects participation and function within daily life. Our two guiding research questions for this study were:

- What does it mean for individuals to be “Barth Tired”?
- How does fatigue impact the daily lives of BTHS individuals?

This study was part of a larger project aiming to qualify fatigue and its impact on affected individuals and their families, as well as quantify fatigue through a biometric data collection device and “real time” reporting of fatigue levels.

Methods

Research Design

We approached answering our research questions using a qualitative research design with a phenomenological approach. Phenomenology was the epistemological approach chosen since our goal was to understand the experiences of BTHS individuals and the meaning, or impact, fatigue had on their daily lives. Data collection was achieved through interviews with affected individuals; interviews were conducted using the zoom video conferencing platform (Zoom video communications Inc.) All research activities, including consent and assent procedures, were approved by the sponsoring university's Institutional Review Board (IRB, study number HM20021612). All participants over the age of 18 provided written consent *via* docusign software. Parental written consent was also obtained using docusign for all participants under the age of 18. Written assent from participants aged seven and older was obtained using docusign software and verified verbally during the interview process. For children under the age of seven only verbal assents was given.

Sample

English-speaking individuals over the age of five with a genetically confirmed BTHS diagnosis were recruited using a purposive convenience sampling method. Individuals with severe comorbid physical disabilities (*e.g.*, cerebral palsy) were excluded from this study in an effort to maintain the validity of the information gathered as it related to BTHS-specific fatigue as opposed to fatigue as a result of other physical disabilities. Informational flyers were sent *via* the Barth Syndrome Foundation (BSF) listserv as well as posted on the BSF website. A roundtable discussion about fatigue and the research project was also sponsored by the BSF; attendance was free and voluntary, and a recording of the roundtable discussion was posted to the BSF website. Interested parties were able to contact researchers directly *via* email to express interest in participating and to schedule an interview. Some individuals were also recruited following their family member's participation in an earlier phase of the project. Data collection occurred over a period of ~8 weeks until the team reached a point of saturation, meaning that no new themes were emerging from the data.

The final sample included twenty individuals (19 males, 1 female) who met eligibility criteria and completed consent/ assent proceedings. Participants ranged in age from 5 years to middle adulthood; the mean age of our sample was 20 years, 9 months (note: Exact ages of adult participants are removed due to the limited number of adults with BTHS and the high risk of participant identification). Eight of the participants were children ages 5-12 years old, four were adolescents ages 13-17 years old, and eight were adults aged 18 years or older. Our sample consisted of 14 individuals residing in the United States, 2 in Australia, 2 in the United Kingdom, 1 in the Netherlands, and 1 in South America.

Data Acquisition

Interviews

Qualitative interviews were conducted virtually over an eight-week period. All interviews were conducted using the secure video-conferencing platform zoom, which met all IRB standards for security and confidentiality of participant information. All interviews were video and audio-recorded through this application and stored on a secure drive accessible by the research team only. An eligibility screening was conducted via phone prior to each interview.

Interviews were conducted by a trained researcher using a semi-structured approach to encourage the possibility of eliciting unplanned information from participants detailing their unique experiences with BTHS and BTHS-related fatigue. During each interview the questions outlined in (Table 1) were used to guide the conversation; participants were offered follow-up questions and asked to elaborate further on specified experiences. For example, if a participant was asked how fatigue influences their ability to do things that are important to them and they answered that it keeps them from being able to go out to lunch with their friends, the interviewer would then follow-up with probes such as "Tell me more about similar social activities you are unable to engage in due to fatigue".

All participants in the 5-12 age categories were accompanied by one or more parents during the interview that often helped the researcher probe by adding familiar context and personal examples. For example, if the researcher asked the participant "When do you notice fatigue the most?" and the participant stated they were unsure or could not think of an example, the parent may probe with "What are some activities you do at school that you tell me make you tired?" or "What do you do on Saturday mornings that you tell me makes your muscles hurt?". Parents were explicitly instructed not to answer on behalf of their child; but probing and support of the child (especially younger children) was encouraged. A total of 18 individual interviews and one interview with a pair of affected siblings were completed, transcribed, and used in data analysis.

Question	**Optional Probes/Follow-Up Questions**
When I say the word "fatigue", what are the first words or images that come to your mind?	Does fatigue mean something different than tired to you?
	Are there any other words that you are thinking of?
How do you describe "fatigue" or tiredness to your friends or colleagues?	Does this differ from how you would describe it to your teacher, boss, or a stranger?
	Do you think they understand what you are really feeling?
When do you notice fatigue the most?	Related to specific activities?
	Related to time of day?
	Meaningfulness of the task?

	Do you notice the fatigue before others?
How has fatigue influenced your ability to do things that are important to you?	Work/play/leisure?
	Social?
	Self-care?
How has fatigue influenced your relationship with others?	Do you ever say no to hanging out with others because you are too tired?
	Do you ever think people are upset with you because you couldn't do something with them or for them?
	Do you tell people when you are fatigued?
What do you do when you are fatigued?	Do you rest?
	Do you keep going even if you're tired?
	Are there any medications you've tried that have helped with fatigue?
	Are there other non-medication strategies that are helpful?
What else do you think people should know about fatigue or tiredness in Barth syndrome?	

Table 1: Interview Questions and Probes

Data Analysis

Immediately following each interview, audio recordings were sent to Rev.com San Francisco©, a speech-to-text services company for transcription. Each interview was transcribed using Rev's automated transcription service and then read and checked for accuracy against the original audio files by the first author. All identifiers (*i.e*., names, places of residence) were removed from the transcribed files. Once transcription and deidentification was complete, all text files were imported into Atlas.ti, a qualitative research software program. The reviewed transcripts were then read and re-read by two team members (IB and ED). The analysis procedures occurred in an iterative fashion where we interviewed, analyzed, discussed, and repeated the process until data saturation was reached.

The research team met virtually *via* video-conference weekly to discuss collective impressions of the data and monitor that all study procedures were being adhered to. A preliminary code sheet was developed, and two researchers (IB and ED) selected a sample of five transcripts then coded each of the transcripts individually to develop interrater agreeance. Upon coding completion of the sample of five transcript documents the interrater agreement was calculated to be 80.2%. Following coding of the initial five interviews, the researchers met again to discuss findings and refine the coding frames. Each of the refined codes that were selected to be a part of the final coding framework (Table 2) were developed to best qualify the participant's specific lived experiences with fatigue as indicated during each of the interviews. Using the agreed upon coding framework IB and ED coded all transcripts using the Atlas.ti platform and met a final time to verify coding and begin analyzing how the codes informed the development of the themes of the dataset.

Code	**Operational Definition**
Age-Fatigue Relationship	Related to the progression or regression of fatigue over the lifespan
Barth Tired/Barth Fatigue Means	Relating to any aspect of BTHS that insight feelings of tiredness or fatigue.
	Also may include comparisons of what it feels like physically, mentally or emotionally to be tired or fatigued with BTHS.

Comorbidities/Co-occurring Health Issues	Related to the mention of other health defects experienced by the BTHS individual
Development of Self-Awareness	Related to the development of understanding of the self-including but not limited to: personal limitations, preferences, abilities, values, and behaviors
Emotional Impact	The net effect of any aspect of BTHS fatigue on the individuals emotional state including mood and feelings
Family Impact	The net effect of any aspect of BTHS fatigue on the individual's family or individual family members
Fatigue Management/Accommodations	Accommodations: Pre-planned arrangements or agreements made by the BTHS-individual or on their behalf to facilitate engagement.
	Fatigue Management: The physical actions taken specifically to conserve energy.
Inability to Engage in Physical/Meaningful Tasks	Specifically related to the inability to do or engage in a desired activity or task requiring some sort of physical capability outside of the given ability/range of the individual
Limited Independence	Related to the inability to do or engage in a desired activity, task, or relationship due to fatigue
Mental Impact/Fatigue	The net effect of any aspect of BTHS fatigue on the individual's mental state
Planning	The action or process of making an actionable plan or arrangements related to the expectation of ensuing BTHS-fatigue
Response to Fatigue	The strategies used or actions taken specifically in response to experiencing BTHS-fatigue
Signs/Symptoms of Barth Fatigue	The physical manifestations indicating BTHS-fatigue, can be before, during, or after
Social Impact	The net effect of any aspect of BTHS fatigue on the individual's community/social system (family, friends, peers, community)
Triggers	Relating to a specific cause or catalyst of fatigue in an individual with BTHS

Table 2: Code Directory

Results

Our inductive coding process and thematic analysis led to the extraction of four primary themes related to the impact of fatigue on individuals with BTHS.

- BTHS fatigue has significant social implications
- BTHS fatigue manifests itself through cognitive and physical signs and symptoms
- BTHS fatigue is correlated with an inability to engage in activity leading to limited independence
- BTHS fatigue requires fatigue management and accommodations

Once research team members agreed on these key themes, two participants from each age group (*i.e.*, child, adolescent, adult) were contacted *via* email for member-checking. Participants were asked whether each key theme resonated with their experiences having BTHS. This process was used to further corroborate the credibility of the results of the data analysis. All four themes were validated with 100% agreement from participants. Each theme is described in proceeding text.

BTHS-fatigue has a significant impact on opportunities for social engagement among BTHS individuals.

Narratives provided by BTHS individuals suggest that their social opportunities with both friends and family were significantly limited by Barth-related fatigue. Sixteen of our 20 participants discussed the impact of fatigue on their collective social networks (friends and family). More specifically, these participants pointed to an inability to attend or engage in social gatherings and events due to the occurrence, or expected occurrence, of BTHS-related fatigue. One adult participant recounted his struggles with socializing even from a very young age due to his fatigue stating: “All the boys would, you know, play soccer, you know, after classes and I would never join them. Never and that was a social, you know, that, that had implications in socializing.” This trend of limited social opportunities due to fatigue was common among adolescent participants as well. One adolescent participant acknowledged his BTHS-related fatigue as very limiting in his physical ability to keep up with his peers stating: “It's just that more like, I can't keep up with my friends… sometimes my friends come over on their bikes and I can't go with them because just riding a bike is too tiring for me.” Furthermore, another adolescent participant discussed his hesitancy to even try to participate socially for fear of having to explain his BTHS fatigue and consequently becoming an outcast among his more typical peers: “I’m not going to walk around and tell everybody. You know, they might make fun of me.” he stated.

Most participants indicated that their family members and close friends were fairly understanding of their condition and subsequent limitations. However, multiple participants reported choosing not to attend certain events because they did not want to limit others due to their fatigue or be a burden. One adult participant specifically discussed the fact that there are times in which he has declined invites to family events because of anticipated fatigue: “I have sometimes, um, decided like not to go on family vacations”.

BTHS-fatigue is manifested through cognitive and physical symptoms

Through participant interviewing it was revealed that many affected individuals felt that BTHS-related fatigue is more than just “being tired”. When participants were asked what it was like to experience “Barth Tired” or “Barth Fatigue” many indicated an extreme state of both physical and cognitive exhaustion that surpassed a “Typical” level of fatigue, given the activity. One adult participant likened this descent into a deeper level of fatigue to a weight with a heaviness that “pulls you down”. Eighteen of the 20 participants endorsed BTHS fatigue/tiredness as something different than what they perceived typical or everyday fatigue to be. An example of a normal activity causing fatigue in a participant is described in the following text:

I remember as a kid, if I would wear it, a hooded sweatshirt for too long. Yeah. I’d feel the strain in my back, you know, I would quit wearing coats with hoods or jackets with hoods because they would, you know, after a while fatigue my back.

Interestingly, symptoms of cognitive fatigue were mentioned nearly as many times (11 quotes mentioned by 8 participants) by just as many participants as physical fatigue (12 quotes by 8 participants). When describing BTHS related fatigue the most common cognitive symptoms were a slowed ability to think, trouble maintaining focus, and headaches occurring after sustained attention to task. Physical symptoms discussed by participants included burning/soreness in the muscles, intense overall weakness causing the body to feel heavy, and shortness of breath. One adolescent participant described his experience with the Barth fatigue and the limiting nature of such intense physical symptoms: “If I overexert myself, my muscles feel like they're on fire and they burn and hurt… One example that I always bring up is me and my friend went to the pool one day and went off the high dive about like ten or so times before my muscles just absolutely burned up and I was exhausted”. Markedly, five of the six participants who referenced experiencing the burning sensation in their muscles as a specific indicator of BTHS-related fatigue were children. The single adult participant who reported experiencing a similar burning sensation also reported feelings of extreme muscle weakness which he explained in physical terms as well: “It feels like your skin is just kind of stretched over the bones. Like there's nothing there, kind of holding it up”.

BTHS-fatigue often leads to an inability to engage in physical and/or meaningful activities contributing to limited independence

Another key theme that emerged from this project is that individuals with BTHS perceive fatigue as limiting their ability to engage in meaningful tasks, which subsequently influences and inhibits their desired level of independence. An analysis of the interview transcripts revealed that within the sample of BTHS adults interviewed, the most frequent reports of limited independence were related to working, driving, and education. One adult explained: “I can't work so that, you know, that limits your independence quite a bit. there are just a lot of things I just don't feel like up to doing, because I'm tired or know that, you know, I might get a good 30 minutes of work in, and then I'm going to have to stop to take a break or take a nap or something like that”. Another adult participant noted, “The reason I don't work full time is because I, I don't know. I don't know how, what kind of effect that would have on me”. Other limitations attributed to fatigue included travel, with one participant noting: “Of course I would like to impress my girlfriend and all that, but I mean, I, I wasn't able to move. I wasn't even able to carry my own body, let alone the bags to the airport”.

Children and adolescents living with BTHS mentioned limited independence most often in relation to extracurricular activities at school and the community or in terms of completing self-care tasks. One younger participant stated: “Because I get tired…I get dressed with help by daddy or mommy.” Independence with functional mobility was also discussed, with some children needing help ascending/descending stairs, or walking independently for long distances. An adolescent noted: “I mean, it's hard to, you know, do anything. I mean, you know, even going up and down the stairs, you know, it's just, you know, it's just terrible”.

Fatigue management and accommodations in relation to BTHS Fatigue

During the interview process, many participants reflected on the additional planning and preparation required accounting for the unpredictable yet profound nature of BTHS-related fatigue in their everyday lives. Individuals with BTHS-related fatigue described setting up accommodations and fatigue management strategies as paramount to participating in "normal" day-to-day activities such as going to school or hanging out with friends. Eighteen of the 20 participants validated this theme through their comments and stories, indicating that this is a theme that resonates across the lifespan. Specifically, BTHS-affected individuals indicated that a significant portion of their time is spent planning, managing, and finding ways to accommodate for their BTHS- related fatigue (or the expectancy of about of fatigue) at some point during any given outing or activity.

Accommodations were defined in this study as pre-planned arrangements or agreements made by the BTHS-individual, or on their behalf, to facilitate engagement. For example, some adult participants detailed accommodations they used when attending events "It's been a long time since I've been to like a professional sports game or anything like that" one participant stated, "But the deal was, you know, we have to be able to find a handicap parking spot, um, and, you know, just kind of find a way if I go to, uh, an, an amusement park or like, uh, like we have a really famous big garden, um, out here that, uh, we like to go to, uh, probably a few times a year, I get a wheelchair or a scooter or whatever is available." The younger participants tended to refer to accommodations they used in school to avoid physical or cognitive fatigue while attempting to facilitate success. "In gym, instead of running on the blue line I run on the yellow line by myself. And I only do two laps or one instead of three" one younger participant stated. Another school-aged participant noted "I have a roller bag because carrying my bag was too tiring". One adult participant also recalled his experience with certain accommodations in the school setting that have carried over into his adult life "When I was a kid, I had a second set of books. I had books, in home books, at school, and things like that. I still, you know, if I can find it in lightweight alternatives, I tend to pick those ones out."

In this study fatigue management referred more specifically to the physical actions taken by participants to conserve energy. One adult participant detailed the need for consistent scheduling of his days to maintain his productivity without crashing due to overexertion: "I split my day in two parts. I have the morning part and then I sleep for two hours in the beginning of the afternoon and then I have the second part of the day". Across all participant age groups fatigue management was related most often to the need for taking breaks/resting, sleeping, and meticulous diet planning to avoid overexertion and extreme fatigue.

Discussion

The purpose of this study was to gain insight as to how individuals with BTHS experience fatigue and how that experience affects daily function and participation. This is the first study of BTHS-related fatigue which aimed to understand not just aspects of physical fatigue in BTHS but also the mental and emotional facets of fatigue and incorporate them into the full picture of what it means to be "Barth Tired". Findings from this study suggest BTHS-fatigue is pervasive across the lifespan and across areas of daily functioning, often resulting in an inability to engage both physical and social activities resulting in limited independence across the lifespan. Furthermore, across all interviewed age groups, the pervasiveness and frequency of BTHS-fatigue was reported to often require a high-level of planning or modification in order to fully participate.

While literature has documented cases of impaired endurance and muscle fatigue in BTHS individuals [15,18-20,25] findings from this study suggest cognitive or mental fatigue as an additional limiting factor in daily functioning for these individuals. When discussing mental fatigue participants specifically pointed to difficulty maintaining concentration, ability to focus, and memory. Participants indicated that difficulties with these cognitive processes were significantly impactful in relation to work, school, and participation in desired leisure activities/hobbies.

The results of this study provide foundational information for understanding the impact of fatigue from childhood through adulthood in BTHS. As such, it contributes to the natural history of the disorder and provides possible targets for advances in clinical practice and in the future design of therapeutic trials aimed at treating BTHS. The nature of this qualitative study allowed for the person-centered identification of fatigue-related factors most relevant to the lived, objective experience of those with BTHS. As noted by the Patient Centered Outcomes Research Institute (PCORI), patient centered research is inclusive of an individual's preferences and needs, focusing on outcomes that people notice and care about such as function, symptoms, and health-related quality of life.

In considering the future clinical trials for BTHS, information gained from this study can guide the selection of outcomes measures specific for individuals BTHS. Specifically, this study provides initial evidence that fatigue in BTHS is multi-faceted and not confined to physical fatigue or difficulties with physiological endurance. Our findings suggest that physical fatigue may need to be considered not only in terms of muscular endurance, as previously captured using measures such as the 6MWT and Sit-to-Stand Test (SST), but in a more robust fashion to capture the impact of physical fatigue on social participation, self-care independence, and quality of life. Additionally, future clinical studies should consider including measures of cognitive or mental fatigue since these areas are important to patients and impact participation in meaningful tasks.

In terms of clinical practice, these results serve as a resource for clinicians to better understand how fatigue manifests differently in clients with BTHS compared to more common conditions that are neuromuscular or biomechanical in their origin. Information gleaned from these interviews may be used by clinicians to guide selection of energy conservation techniques, accommodations, and task-modifications for optimal participation across settings and context.

Limitations and Conclusion

In considering the results of this study it is important to acknowledge possible limitations of the research design and overall study. First, recruitment occurred through the Barth Syndrome Foundation (BSF). There is a possibility that those who are not registered with the foundation or who have undiagnosed cases of BTHS may experience fatigue differently than those individuals who participated in this study. As such, key themes generated from our analysis may not represent all individuals with BTHS. Additionally, this study relied completely on self-report data which is inherently reliant on introspective ability and honesty which is difficult to assess for accuracy. There is a chance that instances of personal bias or a desire to give more socially acceptable answers to the interview questions rather than truthful responses were present. However, self-report data was deemed an appropriate method of data collection given the objectives of this study were to better understand how individuals with BTHS experience fatigue and the impact it has on their daily lives. Despite these challenges, this study serves as an initial step in discovering more about the relationship between fatigue and energy expenditure in relation to BTHS. This study yielded valuable responses from participants that shed light on their BTHS-fatigue; providing important direction for future research and the ultimate goal to be able to provide treatment for individuals with BTHS that specifically addresses BTHS fatigue as a way to improve these individuals' quality of life.

Acknowledgment

The research team would like to thank Dr. Erik Lontok, scientific director of the Barth Syndrome Foundation (BSF), and Shelley Bowen, former chair of BSF and current director of Family Services and Advocacy (FSA), for their help with subject recruitment and study design. We would also like to thank the participants and their families who gave their time to this study. This research was supported by an Idea grant from the Barth Syndrome Foundation (BSF) (NIH R41) and the use of REDCap was made possible by award number UL1TR002649 from the National Center for Research Resources (NCRR).

Conflict of Interest

The authors have no conflicts to declare.

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